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REMARKS

Prior to this communication claims 1-8 were pending. By the present communication, new claims 57 and 58 are added and claim 1 has been amended to define Applicants' invention with greater particularity. The amendments add no new matter, being fully supported by the Specification and original claims. Accordingly, claims 1-8, 57 and 58 are currently pending

The Drawings

The drawings are objected to for the reasons listed on Form PTO-948, namely for allegedly having numbers and reference characters not plain and legible, poor figure legends, and for lacking sufficient margins. Since PTO-948 lists only informalities and drawing corrections are not requested. However, to be responsive to the drawings objection, Applicants submit herewith as Exhibit B formal drawings containing corrections of the noted informalities. Accordingly, reconsideration and withdrawal of the objection to the drawings are respectfully requested.

The Objection to the Specification

Applicants respectfully traverse the objection to the disclosure for alleged informalities. With regard to the objection based on failure to submit nucleotide and/or amino acid sequence disclosures, Applicants submit herewith a Sequence Listing with a computer readable copy and a

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Statement verifying that the Sequence Listing adds no new matter as required by 35 C.F.R. §1.821-1.825. With regard the objection to the abstract for containing the phrase "activities a protease" when the phrase "activates a protease" should have been used, by the present communication Applicants have amended the Abstract to correct this inadvertent error. Applicants submit that the grounds for objection to the Specification as containing informalities are now overcome and reconsideration and withdrawal of the objection are respectfully requested.

The Rejection Under 35 U.S.C. § 112, Second Paragraph

Applicants respectfully traverse the rejection of claims 1-8 under 35 U.S.C. § 112, Second Paragraph as allegedly being indefinite. With regard to the phrase "or active fragment thereof" in claim 1, the Examiner asserts that it is unclear whether the phrase refers to the antibody, the transcriptional activator, the enzyme, or all three. To clarify that the phrase refers to the antibody, claim 1 has been amended to recite "an antibody or active antibody fragment."

With respect to the term "operatively" as used in claim 1, the Examiner asserts that it is unclear whether the term is meant to limit the claim or make clear some aspect of the claim. The term "operatively linked" is described in the Specification as meaning "a juxtaposition wherein the components so described are in a relationship permitting them to function in their intended manner (Specification, 15, lines 22-24). However this definition is set forth in the context of a discussion of polynucleotides, rather than proteins. Accordingly, to remove any lack of clarity

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inadvertently introduced by the term "operatively", claim 1 has been amended to delete the term at issue.

In view of the above-described amendments to claim 1, Applicants submit that all pending claims meet the requirements of 35 U.S.C. § 112, Second Paragraph.

The Rejection Under 35 U.S.C. § 112, First Paragraph

Applicants respectfully traverse the rejection of claims under 35 U.S.C. § 112, First Paragraph as allegedly containing subject matter that was not described in the Specification such that those of skill in the art would understand that Applicants had possession of the claimed invention at the filing of the application.

A. With regard to the rejection as separately applied to claims 1-4 and 7, the Examiner asserts that the newly added claim limitation "wherein said reporter is an antibody or active fragment thereof" is not supported by the original disclosure and, therefore, constitutes new matter. The Examiner acknowledges, however, that the "reporter" may be a polypeptide that contains an epitope that can be bound by an antibody (Office Action, page 5). By the present communication, claim 1 has been amended to replace the phrase "wherein ...said reporter is an antibody or active fragment thereof" with the phrase "wherein ...the reporter is a polypeptide having an epitope that can be bound by an antibody, or active antibody fragment", thus removing the grounds for the rejection.

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B. With regard to the rejection as separately applied to claims 1, 2, 5, 6 and 8, the Examiner asserts in support of the rejection that the rejected claims "are directed to all possible fusion proteins comprising a repressor polypeptide that represses the activity of a reporter polypeptide" (Office Action, page 5). However, the Examiner acknowledges that the Specification provides "representative species" of fusion proteins "comprising a reporter [*sic*] polypeptide which confers a specific localization in the cell such that the attached reporter has reduced activity" (Office Action, page 5). (Applicants assume that the Examiner misspoke and meant to say that the *repressor* polypeptide confers a specific localization in a cell to cause reduced activity of the reporter polypeptide. If this assumption is incorrect, Applicants request the Examiner to contact their representative by telephone to discuss the rejection.) In addition, the Examiner acknowledges that Applicants provide "an enabling disclosure for fusion proteins comprising a repressor polypeptide that confers a specific localization in the cell such that the attached reporter has reduced activity" (Office Action, page 6).

By the present communication, claim 1 has been amended to require "a repressor polypeptide that represses the activity of the reporter polypeptide by conferring a specific localization in a cell such that the reporter polypeptide has reduced activity". Support for the new claim language is found in the Specification at page 13, lines 18-19.

Thus, Applicants respectfully submit that all grounds for the rejections under 35 U.S.C. § 112, First Paragraph, have been removed and Applicants respectfully request reconsideration and withdrawal of the rejections.

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In view of the above amendments and remarks, Applicants submit that all rejections and objections have been overcome. Reconsideration and favorable action on all claims are respectfully requested. If the Examiner would like to discuss any of the issues raised in the Office Action, the Examiner is encouraged to call the undersigned so that a prompt disposition of this application can be achieved.

Respectfully submitted,

Date: November 18, 2002



Lisa A. Haile, J.D., Ph.D.

Registration No.: 38,347

Telephone: (858) 677-1456

Facsimile: (858) 677-1465

USPTO CUSTOMER NUMBER 28213
GRAY CARY WARE & FREIDENRICH LLP
4365 Executive Drive, Suite 1100
San Diego, California 92121-2133

Enclosure: Exhibit A
Exhibit B – Corrected Formal drawings (Figures 1-4)

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Exhibit A: Page 1

EXHIBIT A
Version with Markings to Show Changes Made

In the Specification

Please replace the Abstract on page 51 of the Specification with the following new paragraph:

-- The invention provides a fusion protein including a reporter polypeptide, a linker polypeptide comprising a protease cleavage site, and a repressor polypeptide. The repressor polypeptide can repress the activity of the reporter polypeptide by conferring a specific localization in a cell that reduces activity of the reporter activity until the cleavage site is cleaved. A method is also provided for identifying a protease that recognizes a specific protease cleavage site. The invention further provides a method of identifying a compound that activates a protease. --

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Exhibit A: Page 2

In the Claims

Please amend claim 1 as follows:

1. (Thrice Amended) A fusion protein comprising:
 - a) a reporter polypeptide linked to a linker polypeptide comprising a protease cleavage site;

wherein said reporter polypeptide is an enzyme, a transcriptional activator, or [an antibody or active fragment thereof] a polypeptide having an epitope that can be bound by an antibody or active antibody fragment; and
 - b) a repressor polypeptide that represses the activity of the reporter polypeptide by conferring a specific localization in a cell such that the reporter polypeptide has reduced activity, wherein said repressor polypeptide is [operatively] linked to the linker polypeptide, and

wherein cleavage of said linker polypeptide at said protease cleavage site increases the activity of said reporter.

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Exhibit A: Page 3

Please add new claims 57 and 58 as follows:

-- 57. (New) The fusion protein of claim 8, wherein the reporter polypeptide is a transcription factor.

58. (New) The fusion protein of claim 1, wherein the inhibitor polypeptide is a transmembrane protein and the linker peptide is linked to the intracellular domain of the transmembrane protein.--